Molecular Biology

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Module - 12

Applications of Molecular Biology

Lecture-50 Applications of Molecular Biology (Part 2)

Hello everyone, this is Dr. Vishal Trivedi from department of biosciences and bioinformatics IIT Guwahati and what we were discussing? We were discussing about the different aspects of the molecular biology in the course molecular biology. So, far what we have discussed? We have discussed about the cell biology, we have discussed about the molecular biology, we have discussed about the central dogma of molecular biology, we have discussed about the transcription, translation, replications, post translational modifications, we have discussed about the cell cycle, cell division, apoptosis and all other kind of aspects. And apart from that we have also discussed about the different types of techniques what has been developed. So, we discussed about the polymerase chain reactions, real time PCR, blotting techniques, we have discussed about the southern blotting, northern blotting and western blotting.

And in the previous module we have also discussed about the genome editing. So, and we have discussed about the different aspects of the genome editing in very briefly we have discussed all these. So, with this we have discussed in detail about all the tools and techniques which are available with the molecular biology. And now it is a time to review to see how these techniques can be utilized for the welfare of the human society.

So, what we have what we have discussed we have discussed about that molecular biology can be can have a extreme potential into a different heels. It can be used for the poultry industry, it can be used for the agriculture, it can be used for generating the transgenic animals, it can be used for developing the recombinant proteins and so on. So, since the scope is diversified we decided that we will focus only on to the four aspects related to the molecular biology. We are going to discuss about the genetic engineering, we are going to discuss about the PCR based applications, we are going to discuss about the transgenic animals and we also going to discuss at the end about the genome editing. And how the genome editing can have the applications in the different types of areas.

Now, in today's lecture we are going to discuss about the transgenic animals. So, transgenic animals so, when we say transgenic animals these are actually the animals where you are

actually going to have the two different types of characters two different types of characters what are present. And transgenic animals are the animals where you are actually going to put the external DNA into the into the particular right. So, transgenic animal means you are actually going to put the genetic content from the trans which means from the outside and that is how it is actually going to modify the particular animal. So, what is the application of the transgenic animals? The application of transgenic animal is that it is actually going to be used for understanding a particular disease mechanism.

So, we will take a few examples then you understand how the transgenic animals are utilizing for developing the different types of disease mechanisms. One of the classical example is the cancer for example. So, if a particular cancer is been developed because the particular type of transcription factor is been required and it is actually over expressing in a large quantity. So, then what you can do is you can just over express that particular transcription factor into a particular animal and that animal is eventually going to develop the cancers of the breast or pituitary or any kind of thing. So, that can be used for studying the how the cancer is been developed and that can also be used for the studying the or exploring the anti cancer drugs also.

Then it also be can be used for studying the normal physiology. So, just like as we discussed for the cancer it can also be used for studying how the blood clotting is working, how the the nerve conduction is working, how the all the muscle contraction all those kind of. So, because all these mechanisms are requiring the different types of factors. So, if you remove one or two other factors it can be help you to understand what will be the role at that particular factor. For example, if you remove the actin and if you remove the myosin or if you remove the some crucial GTPases it will tell you that ok, this is the function of the particular protein and that is how this is going to help you understanding the normal physiology.

Then it also can help you in producing the biological products. So, biological product where you actually can produce or you can actually be able to generate a transgenic animals and that is good in giving you a particular desirable product. Then it also can be used for vaccine development and it also can be used for the toxicity testing. For example, toxicity testing in in those cases where you cannot test the particular product directly onto the human, but you can actually be able to develop the humanized animals, you can be able to develop the transgenic animals which are actually going to mimic the physiology of the humans, but they are not humans and then you can actually be able to do the toxicity testing in on those animals. So, as far as the transgenic animal is concerned transgenic animals could be of two types.

It could be a animal where you are over expressing a particular gene or it actually can be a transgenic animal where you are actually going to remove a particular gene. So, when you are over expressing a gene you are expressing a gene into a suitable vector and these kind of transgenic animals are always been used for the organ transplant. Compared to that

when you are doing the knockouts you are removing a particular gene expressing functional gene and this is useful for understanding the role of that particular gene into a particular process. For example, cancer development, normal physiology and all that. So, first understand the disease mechanism.

So, we will discuss about the transgenic animals and how they are been exploited to exploring the different types of aspects related to molecular biology or other biochemistry fields. So, first is the transgenic animals which are been used for understanding the disease mechanism. So, you can actually have the disease model, you can have the disease model like conventional method where you are actually going to treat a particular animal with a particular type of treatment and that is how it is actually going to have the conventional method. So, in the conventional method what will happen is that you are actually going to treat the animals with like for example, you can actually be able to treat animal with a mutagenic compound. So, if that will happen then it is actually going to cause the mutations or you can actually be able to use the chemicals and that is how it is actually going to cause the development of particular disease.

For example, if you treat the rats with the streptomatose gene it is actually going to develop the diabetes mellitus. Similarly, you can actually be able to use the some kind of physical method. For example, you can actually be able to use radiation and if you radiate a particular organ that organ is actually going to be disappeared and that is how you can be able to develop a disease model. For example, when people have discovered the diabetes right they actually literally remove the pancreas of a particular animal. So, when they when they remove the pancreas from the dogs they found that the dogs are developing the diabetes and that is how these are actually are the conventional method.

What is the limitation of this? That limitation is that there will be no precise control you are actually removing the pancreas. So, if you are removing the pancreas you are not removing only one you are removing a complete organ and that complete organ may have the some more functions right it may just not have the function of reducing the insulin it is also going to have the other kind of effects. Then it also going to cause the gross changes in the physiology right. So, gross changes in the physiology you do not know that if it is directly or indirectly affecting that particular process. Then it may contribution of the multiple organ it could be possible that there could be a contribution of multiple organ in that particular process and you may be just removing one organ or two organs and that is how.

So, to avoid these kind of complications people are developing the transgenic animals. So, that you can very precisely be able to say that ok, the effect of actin in this process is this effect of myosin is in this process is this. So, that is one of the advantage of developing the transgenic animals. So, genetically altered animals where you are either going to over express or knock out to resemble the signature pattern of a human disease conditions. Now, what is the major advantage of developing a transgenic animals? It is target specific

gene site you know that what gene you are trying to you know trying to test right.

So, you can actually be able to do that there is no human subjects involved then it is cheap and quick and it is reproducible. For example, for a disease model like AIDS mouse, alzheimer mouse, onco mouse, diabetes, zebra fish based models and all that they are being developed. Then for example, the AIDS model right. So, no reported case of AIDS in the animal right. So, monkey can get only infected with the SIV.

So, first AIDS mouse model is skid mouse right and the animal used for that model is rat, cat, rabbit and Drosophila. And what is the advantage of animal AIDS model? It is actually cheap, it is much is already known about their genes. So, you know that this animal what is the genetic makeup of this animal and so on. So, it is very difficult it is easy for you to decipher right. And then let us talk about the another model which is called as the Alzheimer's mouse right.

So, it is a neuro generative brain disorder which is where the amyloid plaque or the amyloid beta part peptides fragments of beta are actually going to be accumulated into the brain. And the APP mutation to induce the protein aggregation is the key to develop the AD mouse model right. So, TG2576 is a good transgenic mouse model to start with and in order to produce the genuine human amyloid. Words first Alzheimer mouse incorporated and APP mutations. The pathophysiological effect were similar in the transgenic mouse and it is comparable to the human.

So, Alzheimer disease is a very very serious disease of the central nervous system and it is actually going to be. So, you can actually be able to use these mouse model to screen the compound, you can actually be able to use them for developing the new methods of developing the treatment and so on. And then we have the cancer mouse model. So, cancer mouse models are very very common for example, this is a nude mouse. So, to study the cancer formation and to screen the anti-tumor drugs oncogenes are either mutated to induce the spontaneous cancer formations, knock out of a tumor suppressor gene for example, RB genes or the p53.

Then you can also have the HER2 overexpression and that is also associated with the cancer formation. For example, the HER2 transgenic miles which is called FBB slash N dash MMT new mouse and there are 13 different types of strains which are been engineered to develop the transgenic animals and those in transgenic animals are spontaneously going to develop the cancer. So, they will mimic the natural way of developing the cancer. Then we have a transgenic model for diabetes. So, for studying the gene and their role in peripheral insulin actions, the model of insulin secretion is the glucokinase and the beta receptor knockout mice, uncoupling protein knockout mice and acute and chronic model for the anti-diabetic agents.

Then we also have the zebra fish and the zebra transgenic zebra fish which is for the

cardiovascular disease model. So, these are the some of the cardiovascular diseases for which the transgenic zebra fish model is being developed. And what is the major application of the transgenic animal? They are actually being used for understanding the disease mechanism, normal physiology. So, transgenic animals which are genetically engineered to produce a human pharmaceutical product in their saliva, milk, urine or blood. So, they are being called as farming.

Transgenic animals produce the RPs or the products for example, the milk for example, human anti-thrombin 3. Then we also have the chicken egg white. So, for example, the MAB and human interferon gamma NSH etcetera and insulin which is for the diabetes mellitus. And then we also have the production of vaccine into the transgenic animals like the growth factors, coagulation factors and lactoferrin and the infant formula feed. Then we also use the transgenic animals even for the organ transplant right.

So, organ transplant you know that the you require a donor organ donor person you actually require a suitable organ. So, that it is matching with the acceptors and so on. So, that is a very complicated process. So, and at the end you require a human being to give you the organs right. So, to avoid that you can actually be able to develop the transgenic animals.

So, that you can develop a particular organ or you can actually be able to take directly from that particular transgenic animals. So, transgenic animals for the organ transplants. So, transgenic animals that are genetically modified to have organ that can be transplanted into the human do not express the key foreign antigens. So, you can actually be able to avoid the graft rejections. Then promising the alteration to the human runners pig is the animal used in this process so far.

Why it is so? Because the pig is big in size thus the size of the organ what you are going to get from the pig is probably will be functionally active. And the pig is actually very close to the human being. So, their physiology and their processes are going to be identical or almost similar to the human. So, that is why it is it is been accepted or. So, for example, the porcine heart wall successfully transplanted into the human heart.

Then its physiology is closer matching that of human and that is one of the positive point of developing or transgenic animals especially the pig. And it is much less expensive than the monkey and other primates. So, then it is called as super pig and it is fast growing and lean animals it express the bovine growth hormones. So, super pig is a transgenic animal which is been developed to produce the bovine growth hormones. Then we have the super fish which are called as the aqua advantage salmon and these are the genetically modified Atlantic salmon.

Then we also have the GH regulating gene from the Pacific Chincu salmon. Then we also have a smart mouse. So, smart mouse is a superior learning and memory and the doggy

mouse. So, it is modified to over express the NRF NR2B transgene in the cortex and hippocampus and thalamus and brain stem and cerebellum. So, these are the you know the mouse which are actually having the higher IQ values.

Then this is the transgenic animals and their advantages. So, these one of the major advantage is that the gene requires certain cellular mechanism to help the production of protein. The animal used to trans use for transgenic purposes naturally carry the mechanism needed to produce the complex protein. This mechanism is absent in the cell culture. So, when you try to produce the protein in the same culture it happens sometime that the protein what you are producing at the final stage may not be that much efficient compared to that the protein what you are producing in the transgenic animal.

Because in the transgenic animal naturally it is getting into the another the effect from the vicinity and because of that it is may be more effective. The expression to cell culture or bacterial culture require the constant monitoring and sampling right. Because you are supposed to feed the animals your animal cells you are supposed to do all those kind of thing right. Whereas if you are developing a transgenic animals you are actually animal will do all is that right animal is going to supply the nutrient for the liver animal is going to supply the nutrient for all its organ right.

So, that will be easier. The isolation and the purification of expressed protein in a conventional method is more difficult than the purifying protein from the animal or milk from the body fluid. So, that is also one of the thing right. If you are developing a transgenic animals you can actually be able to have the large quantity of that particular protein compared to that if you want to isolate that same protein from a from a non transgenic animals. It is more cost effective as product is efficiently passed through the milk on a average yield of 53 percent and a 99 percent purity. It has been estimated that the transgenic animals can produce it in its lifetime is 100 to 200 million worth of the pharmaceuticals.

But apart from these the transgenic animals advantages you also have the several disadvantages. For example, the transgenic animal project is extremely expensive. Generation of transgenic animal is also expensive because of the long gestation period, litter size and the higher maintenance cost of the recipient animals. There may be a high mortality rate and other deleterious effect on the animal used by the researcher to create the transgenic breeds. It has been observed that the transgenic pigs have enhanced the growth rate and efficient feed convention exhibit reduced reproductive performance and may suffer from the arthritis and the dermatitis.

Large number of recipient is required to amir transfer because of the low transgenic rate and the transgenic food that has been produced and better productivity in terms of both yield and quantity. However, there are some appreciation about the safety of the transgenic foods. So, one of the major challenge is that many people do not accept those product

because they are coming from the transgenic animals right. So, there are ethical concern, there are the social concern. So, that may be are not accepting these transgenic the product from the transgenic animals.

So, these are the some of the advantages and as well as the disadvantages of the transgenic animals. But molecular biology is being used extensively to produce the different types of transgenic animals and they are very very useful in terms of addressing the or developing the disease models. They are being used for developing the understanding the mechanism of a disease and as well as the normal physiology. So, molecular biology has a immense potential to provide the products for the social welfare.

So, with this I would like to conclude my lecture here. In our subsequent lecture we are going to discuss some more aspects of the molecular biology and we will discuss how the molecular biology can be used for developing the different types of techniques based on the PCR techniques and as well as the genome editing techniques. So, with this I would like to conclude my lecture here. Thank you. .